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ORIGINAL ARTICLE

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Sudden unexpected death in epileptics following sudden, intense, increases in geomagnetic activity: prevalence of effect and potential mechanisms

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Abstract Abrupt, intense increases in global geomagnetic activity during the local night may precipitate a significant proportion of sudden unexpected (or unexplained) deaths (SUD) in epileptics. Over a 2-year period SUD in healthy chronic epileptic rats occurred when the average daily geomagnetic activity exceeded 50 nT (nanoTesla) and suddenly began during local night. Other experiments demonstrated that epileptic rats displayed more spontaneous seizures per night if there had been sudden increases in geomagnetic activity. Analyses of previously published data indicated that the number of SUDs/month in a population of human epileptics was positively associated with the number of days/month when the average geomagnetic activity exceeded 50 nT. The results support the hypothesis that suppression of the nocturnal concentrations of the endogenous anticonvulsant melatonin by sudden increases in geomagnetic activity may encourage fatal cardiac arrhythmias by uncoupling the insular/amygdaloid-paraventricular hypothalamic-solitary nucleus pathways.

Key words Geomagnetic activity · Chronic epilepsy · Sudden unexpected death · Arrhytmia · Melatonin

Introduction

Sudden unexplained (or unexpected) deaths (SUD) have been associated with epilepsy (Leestma et al. 1984) and account for more than 15% of mortality in epilepsy (Schraeder and Lathers 1990). A comparable percentage was noted before the introduction of the current use of anticonvulsants. The risk has been estimated to be between 1:370 and 1:1000 within the general epileptic population (Leestma et al. 1989). When the population is narrowed to match the age and sex of the usual case, the risk could approach 1:200 (Leestma 1990).

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SUD has been reported to occur most frequently in young (median age 32 years) patients who were ambulatory and were employed; the victim was most commonly male and had experienced tonic-clonic seizures for at least 2 to 3 years (Leestma 1990). Approximately 80% of the patients died in their bedrooms, primarily while they were asleep or were entering transitional stages (Terrance 1990). Although the most common trigger for SUD in epileptics has been attributed to ethanol abuse, sleep deprivation or withdrawal from (or non-compliance with) medication, there is now compelling evidence that sudden increases in geomagnetic activity and subsequent suppression of nocturnal levels of the endogenous anticonvulsant melatonin within the epileptic brain may precipitate some SUDs.

Decreases in convulsive thresholds during periods of enhanced global geomagnetic activity have been reported in large populations of epileptics (Keshavan et al. 1981; Rajaram and Mitra 1981). Intense subjective experiences, the phenomenology of which are very similar to the hallucinations sometimes accompanying paroxysmal activity within the subcortical (amygdaloid-hippocampal) portions of the temporal lobes (Horowitz and Adams 1970), are also more likely to occur when daily average antipodal (aa) indices (Mayaud 1973) for perturbations in the geomagnetic field exceed 20 to 30 nT (Persinger 1988; Randall and Randall 1991). Above this threshold pharmacological treatment for status limbic epilepticus in rats has been shown to be less effective (Bureau and Persinger 1992).

The incidence of geomagnetic storms, when daily aa values range from 30 nT to >100 nT, has been related to solar activity and to shock events at the boundary between the earth and the interplanetary magnetic field (Legrand and Simon 1985). One category of geomagnetic activity, which has theoretical relevance to biological systems, is sudden storm commencement (ssc). It displays one of the fastest derivatives (change in intensity per unit time) and frequently precedes sudden increases in geomagnetic perturbations. Mayaud's (1975) analysis of 100 years of geomagnetic activity has indicated that

89% of sscs displayed an increase time of 2 to 6 min (the statistical mode was 4 min) with amplitudes of between 5 and 30 nT. It was concluded that the most violent geomagnetic storms were always short (1 or 2 days) and always began with ssc. The rate of change or derivation of the magnitude is potentially important because some tissue, such as the pineal organ, can respond to eddy currents induced by sudden shifts in magnetic field intensity and/or direction (Lerchl et al. 1991a).

The sensitivity of the organism to sudden increases in geomagnetic activity has appeared to be greater during the local night (Kavaliers et al. 1984; Ossenkopp et al. 1983). Laboratory experiments have shown that melatonin is synthesized from serotonin in the pineal organ by the light-sensitive enzyme serotonin *n*-acetyltransferase (SNAT) and by hydroxyindole-*O*-methyltransferase (Foley et al. 1986). Circulating nocturnal melatonin is more than 10 times, and sometimes up to 100 times, higher than day-time levels and peaks occur between local time 0200 and 0600 hours. The rapid eye movements (REM) or dream periods, which are considered as periods of microseizure activity (Stevens 1982), have been associated with transient decreases in circulating melatonin concentrations (Foley et al. 1986) in healthy volunteers. The highest incidence of premature ventricular beats (PVB) has also occurred during REM sleep between 0200 and 0600 hours in patients with known cardiac anomalies (Rosenblatt et al. 1973). It may be relevant that "temporal lobe epilepsy" was once called "sleep epilepsy" because of its nocturnal .predilection; Spratling's (1904) hourly data for more than 100 000 convulsions have clearly demonstrated a peak incidence between 0200 and 0600 hours local time.

Whole body (or brain) exposure of *c.* 2 h to extremely low frequency (ELF) magnetic fields (Persinger 1980) has been shown to produce reductions in both circulating nocturnal melatonin concentrations and SNAT activity (Lerchl et al. 1991b). Shifting the direction of the geomagnetic field for only 30 min during the local night has also reduced circulating melatonin concentrations to less than 50% of non-stimulated values (Olcese and Reuss 1986). These effects were intensified if the rats were "primed" by antecedent exposure to red light during the nocturnal phase. In fact pineal sensitivity to pulsed static magnetic fields changes during the photoperiod. Both SNAT activity and melatonin concentrations have been maximally suppressed when activation and deactivation of the applied magnetic fields at 1 min intervals (for 45 min) occurred during the mid- to late-dark phase but were not affected during the early dark phase (Yaga et al. 1993).

Persinger et al. (1993) have been studying the long-term neuropathological and behavioral consequences of rats in which limbic seizures had been induced by a single systemic injection of lithium (3 mEq/kg) followed 4 to 24 h later by 30 mg/kg of the muscarinic (cholinergic) substance pilocarpine. The normal mortality within 24 h is minimized and the status is abolished by a single injection of the phenothiazine derivative acepromazine within 30 min of the onset of the overt seizure similar in appearance to a type IV kindling profile of rearing and forelimb clonus.

The rats become chronic epileptics and exhibit spontaneous episodes (about 30 s to 1 min) once per day. Histomorphological analyses, months after the onset of these seizures (Persinger et al. 1993), have shown neuronal drop out within the cerebral cortices and within dozens of subcortical telencephalic and diencephalic nuclei that simulate the condition of patients who are prone to SUD. According to Leestma (1990), 70% of SUD cases (compared to 10% of non-selected epileptics) exhibit gross, visible lesions primarily within either the frontal or temporal lobes. These changes were additional to the typical microscopic anomalies within the hippocampal formation. The pervasiveness of the lesions indicated that a history of convulsions in conjunction with substantial injury within inhibitory regions facilitated the probability of SUD.

Rats in which this pattern of brain damage has been induced experimentally also exhibit occasional SUD despite no obvious behavioral or appetite-induced antecedents. These young male rats of 90–200 days in age were healthy and actively interacting with their cage mates on one day and then dead the next day. Postmortem examinations have revealed no obvious external or internal lesions although enlarged hearts and testicles were not infrequent. During 20 years of research we have never observed normal rats, within this age range, display this type of sudden death.

On the night of an unusually strong, sudden increase in geomagnetic activity in June, 1991, a local SUD occurred in a healthy epileptic man. During this period, patients involved with a local support group and primarily diagnosed as limbic (complex partial-temporal lobe) epileptics with nocturnal or early morning generalized convulsions, reported disruptions of their typical periodicity and an enhanced number of seizures. During this same 72 h period, the chronic limbic epileptic rats in our facility exhibited conspicuous increases in the incidence of spontaneous overt seizures and two sudden deaths occurred. These coincidences were so impressive that a protocol was established to investigate the phenomenon.

Methods

Experiment I

To investigate whether the SUDs were associated with enhanced geomagnetic activity and particularly sudden storm commencements, dates for rats that had died suddenly more than 30 days (despite weight and behavioral recovery) after seizure induction during the years 1988 and 1989 were obtained from our daily log books. During this period we were evaluating the behavioral consequences of chronic epilepsy and none of the rats had been given anticonvulsants. A total of 11 rats met this criterion; all rats died during the night-cycle (1930 to 0730 hours). Eight deaths occurred in 1988 and two occurred in 1989. Only one rat died on any given day and only on one occasion did more than one rat (n=2) die within the same month. None of the other colony rats (n=approx. 500) died suddenly.

During this period *c.* 150 rats, with similar seizure histories, were involved in various experiments but did not die suddenly; all rats were male albino Wistars. The chronic epilepsy had been induced by one s.c. injection of 3 mEq/kg of lithium chloride followed either 4 h or 24 hr later by 30 mg/kg (s.c.) of pilocarpine; within 30 min after the display of rearing and forepaw clonus, 25 mg/kg of acepromazine (Atravet) had been injected s.c. All rats had been between 80 and 100 days old at the time of the injections. Although 21 other rats died during this period, their health had deteriorated slowly and they lost weight, being clearly discriminable from the SUD rats.

Daily aa values for the day of, each of the 4 days before and each of the 4 days after the death were obtained from the monthly Geomagnetic Indices Bulletin (National Geophysical Data Center, Broadway, Boulder, Co., USA). The monthly aa average as well as the lag value in days since the previous ssc were also obtained. Because geomagnetic activity on any given day is positively and moderately correlated with the activity of the previous 2 days and subsequent 2 days, repeated measure analyses of variance (MANOVA) were completed; correlated *t*-tests were employed to discern the source of any significant difference. All analyses were completed by Statistical Progams for Social Sciences (SPSS) software.

Experiment II

Fatal seizures (SUD) would be expected to be catastrophic events that would reflect the extreme end of the continuum of electrical seizures. The effect of geomagnetic activity upon the electrical thresholds for seizures should also be less conspicuous but more frequent when quantitative inferences of these paroxysmal conditions are analyzed daily. To test this hypothesis, two separate groups of chronic epileptic rats were observed, which were 90 days old at the time of the lithium/pilocarpine injection. The rats were placed in the experimental setting only after full recovery, with the exception of spontaneous seizures, from the initial treatment. Food and water were available ad libitum; the light/dark regime was 12:12 h and the local night cycle was 1930 to 0730 hours.

In the first part of the experiment, 4 epileptic male rats were housed in a clear plexiglass cage of dimensions 140 cm (long)×37 cm (high)×37 cm (wide). Vibration, squeaks and activity were recorded at 10-min intervals, 24 h/day for 29 consecutive days beginning 15 January, 1993. Activity was recorded by a photo relay sensor (Radio Shack model no. 49–551) while squeaks (a highly correlated index of aggression) were recorded by an AKG D190 ES microphone through a Lafayette model 63040, two-channel voice reaction time sensor. To detect vibration, the threshold of a vibrations transducer (AKG D190 ES microphone with voice coil physically coupled to cage) was set to respond to the marked thrashing and running activity that occurs subsequent to some spontaneous forelimb episodes. The number of vibrations, squeak and photocell events were stored per 10-min interval for 24 h/day by microcomputers.

Construct validity for all of the three measurements had been verified by recording the group's behavior on videotape for 1 h per night for 15 consecutive nights. The correlation (r) between the vibrational indicator and the occurrence of visually verified seizures was 0.87. Ten-minute intervals that contained no seizure sequences averaged about 1.5 vibrational units. If one running-convulsive seizure sequence occurred during a 10-min interval, the index was about 9 to 11 vibrational units. Only data between midnight and 0600 hours, were used in the analysis because such data involved the major peak of activity and gave minimal contamination from extraneous noises.

In the second part of the experiment, all (n=39) of the male Wistar epileptic rats (150 to 200 days old) in our animal pool served as subjects. They had been injected with the usual lithium/pilocarpine seizure-inducing treatment and then with acepromazine. All of the rats had recovered completely from the initial treatment and at least 2 months had elapsed since the initial induction of the seizure. The rats were removed from their home cages (3 rats/cage) from several different maintenance rooms and housed in single standard wire cages within one side of one of two racks facing each other within the same room; food and water were available ad libitum. The consolidation of rats into a single area was completed in order to standardize any environmental transients, e.g., noise from routine operations, which could differentially affect seizure probability.

The experimental protocol specified that the rats would be monitored 3 times per day (for 10 min each) until at least 1 week after a ssc occurred. Based upon historical averages of sscs, the paucity of sscs during the previous months and the concurrent solar activity cycle, the probability was considered to be increasing that an ssc would occur within the subsequent 2 months. This part of the experiment began on 1 September, 1993.

For part 1, time-lag/lead multiple regression analyses were completed between either: 1) the numbers of vibrations (convulsive patterns), 2) the mean numbers of photocell disruptions per unit time (the index of general ambulation) or 3) the numbers of squeaks (since aggressive behavior is also associated with vibrational movement) and geomagnetic activity (24 h aa values) for the day of and for each of the 3 days before and after the key day. Separate Spearman correlations between the lag/lead values of daily aa activity and either the indices of seizures, general ambulation or intragroup aggression were performed. Partial correlations were completed between the daily aa values and the seizure index after the latter's shared variance with either general ambulation or aggression had been removed. Spearman correlations for the number of limbic motor convulsions during the 30 (3×10 min) observations/day and the lag/lead values of average daily geomagnetic activity were completed for part 2.

Experiment III

To test the hypothesis that clinical cases of SUDEP (sudden unexpected deaths in epileptic patients) were correlated with monthly geomagnetic activity, the monthly variations in the numbers of sudden unexpected deaths in epileptic patients were obtained from Leestma (1990). The numbers of deaths/month for this 2-year period (1983 inclusive and an unspecified 1977–1978 interval) were compared to the 1983 geomagnetic data. If the association between the intensity of geomagnetic activity and SUDEP was robust (and hence have potential clinical relevance), then the correlation with the monthly aa values for 1983 only should be statistically significant. Monthly aa values were obtained from the Monthly Geomagnetic Indices Bulletin. To discern intensity dependence, the numbers of days per month that contained averages of >20 nT, >30 nT, >40 nT and >50 nT were extracted.

Results

Experiment I

As seen in Fig. 1, SUD in rats with chronic epilepsy occurred on days when there was a marked increase in geomagnetic activity compared to the previous and subsequent days. All of the 11 rats died during nights when geomagnetic activity was at least >1 standard deviation above the monthly mean. Nine of the 11 rats died suddenly within 24 h of a ssc; because the incidence of sscs during the months in which these rats died ranged between 2 and 4, the probability is <0.001, that the association between sscs and SUD was due to chance.

Repeated measures analysis of variance was completed for both the absolute and log (base 10) transformations (in order to reduce the heterogeneity of variance between days) of the daily aa values for the day of death and for each of the 2 days before and each of the 2 days

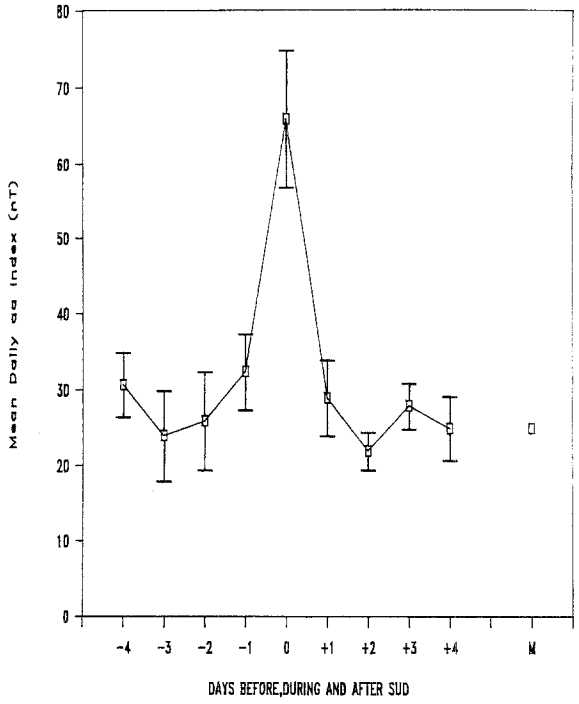

Fig. 1 Average antipodal (aa) values (in nanoTesla) for the days of, the days before, and the days after sudden unexpected deaths (SUD) of healthy male chronically epileptic rats

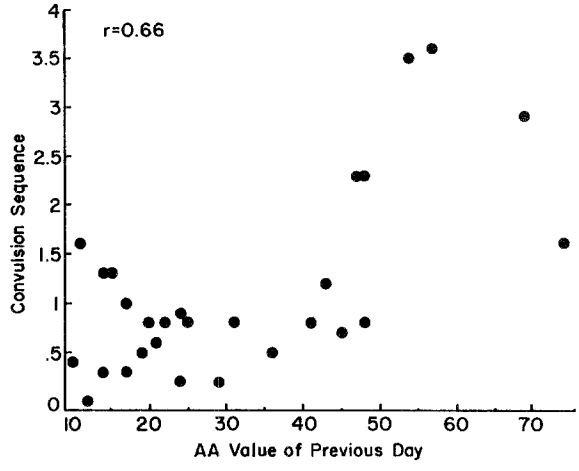

Fig. 2 Scattergram of mean seizure sequence between 0200 and 0600 hours for a group of rats (values >2.0 are equivalent to at least 4 convulsive running seizures that are most associated with cardiovascular irregularity) and the daily aa values of the 24-h period that preceded and overlapped the measurement intervals. (*AA* Average antipodal indices)

after the death. The elevation in geomagnetic activity during the 24-h period of sudden death was statistically significant [$F_{4,40}$=7.96, 6.77; P<0.01] for both aa values and the log (base 10) aa values which satisfied the assumption of homogeneity of variance. The significance was still present for both measures according to the conservative Greenhouse-Geisser estimate (*d.f.*=1.85, 40; P<0.01) and for the extremely conservative lower band alpha value (*d.f.*=1,40; P=0.02).

Correlated *t*-tests indicated that only the increased geomagnetic activity during the 24-h interval of the SUDs was significantly (P<0.01) different from the other 4 days that did not differ significantly from each other. Additional correlated *t*-tests between the monthly average of the aa values and each of the 5 days around the time of the SUD demonstrated that only the geomagnetic activity on the day of death was significantly higher (t(10)=3.35, P=0.01) than the average monthly activity.

To determine if the time of occurrence of the sscs significantly affected SUD, the local time (UT=universal time minus 4 or 5 h, depending upon daylight savings time) was determined for each of the 21 sscs that occurred during the months in which the 9 rats had died within 24 h of these events. Chi-squared analysis (chi-square=4.25, P<0.05) showed that most (7/9) of the rats died if the sscs (11 of the 21) started during the local night (dark cycle). The time-of-day effect was more revealing when the time of day was divided into four, 6-h periods. Chi-squared analyses showed that significantly more (chi-square 10.74, *d.f.*=3, P=0.01) rats (6/9) died if the ssc began during the first 6 h of the dark cycle.

Experiment II

The correlations between the numbers of vibrational patterns that are associated with spontaneous seizures and motor convulsions and the daily intensity of the geomagnetic variation were statistically significant (P<0.01) only with the aa values of the same day (Spearman rho=0.45) and the day before (Spearman rho=0.57) the measures. There were no statistically significant associations between seizure-related vibrational patterns and geomagnetic activity for any of the other days of the lag/lead interval of −3 to +3 days. Similarly there were no statistically significant correlations between lag/lead aa values and either intragroup aggression or ambulatory activity. Removing the shared variance between the general activity (as determined by photocell measurements) or numbers of squeaks and the seizure indices before its correlations with geomagnetic activity did not appreciably change the magnitude of the seizure-geomagnetic correlations or their statistical significance.

The scattergram (Pearson r=0.66, P<0.01) for the numbers of seizure patterns occurring per 10 min between 0200 and 0600 hours and the 24-h aa values during the day before the measurements is shown in Fig. 2. Visual inspection indicated a discontinuity, represented by an increase in seizure events, when the daily aa values exceeded approximately 50 nT. Vibrational measures that ranged between 9 and 11 units per 10-min increment were calibrated visually with one running convulsive sequence. If the background activity ranged between 1 and 2 units per 10 min, a weighted mean of >2.5 units per hour (Fig. 2) indicates that at least one of the 10-min increments contained a value of >10 units. Therefore the numerical values indicate that about one such sequence for the group (of 4 rats) per hour between 0200 and 0600

hours had occurred during nights following a 24-h interval during which geomagnetic activity exceeded 50 nT.

The results of the 2nd part of the experiment were conspicuous. During the 27-day period during which a total of 39 male rats were housed singly and monitored daily, there was only one sudden death. It was during the only night during this period when sudden storm commencements occurred at local time of *c.* 0400 hours. The probability that this death would occur by chance alone on the same night as the single ssc is less than 0.05. The numbers of observed seizures in the population and the daily aa values are shown in Table 1. The strongest and most significant correlation was between numbers of seizures and aa values of the same days as the seizures (rho=0.47; $P<0.01$).

Table 1 Day, number of overt seizures (forelimb clonus, standing and falling) during the 30-min observation period and daily aa values for 39 chronically epileptic rats (*aa* Average antipodal values)

Day	Preliminary aa	Number of seizures	Day	Preliminary aa	Number of seizures
01	4	0	16	7	0
02	4	0	17	6	0
03	34	1	18	5	0
04	32	0	19	5	0
05	12	0	20	17	0
06	11	0	21	0	0
07	9	0	22	7	0
08	7	0	23	8	1[a]
09	5	0	24	13	0
10	6	0	25	9	0
11	5	0	26	10	0
12	10	0			
13	82	3			
14	31	2			
15	17	0			

[a] Day of only sudden storm commencement and only sudden unexpected death during observation period

Experiment III

The conservative Spearman rho analyses (to minimize the contribution from outliers) indicated that only the association between the numbers of SUDEP per month from Leestma's (1990) data and the numbers of days in which the aa values exceeded 50 nT approached statistical significance (rho=0.43, $0.05<P<0.10$). The correlations between SUDEP and the numbers of days per month in which the aa values exceeded 20 nT, 30 nT or 40 nT were not significant statistically. The results are shown in Fig. 3. To differentiate the specific effect of days with values >50 nT, partial correlation analyses were completed between this measure and SUDEP after the mean monthly activity was held constant. The results demonstrated a statistically significant partial correlation coefficient (r) of 0.54 ($P<0.05$) between SUDEP per month and the numbers of very active days (>50 nT) per month. Partial correlation analyses with the numbers of days during which aa values exceeded 20 nT, 30 nT or 40 nT were not significant statistically.

Discussion

The results of these analyses strongly suggest that a significant portion of SUDs in chronic epileptic patients could be precipitated by sudden, intense increases in global, geomagnetic activity. All of the chronic but healthy epileptic rats that died suddenly in our series of laboratory experiments during 1988 and 1989 had succumbed on nights during 24-h intervals when the aa val-

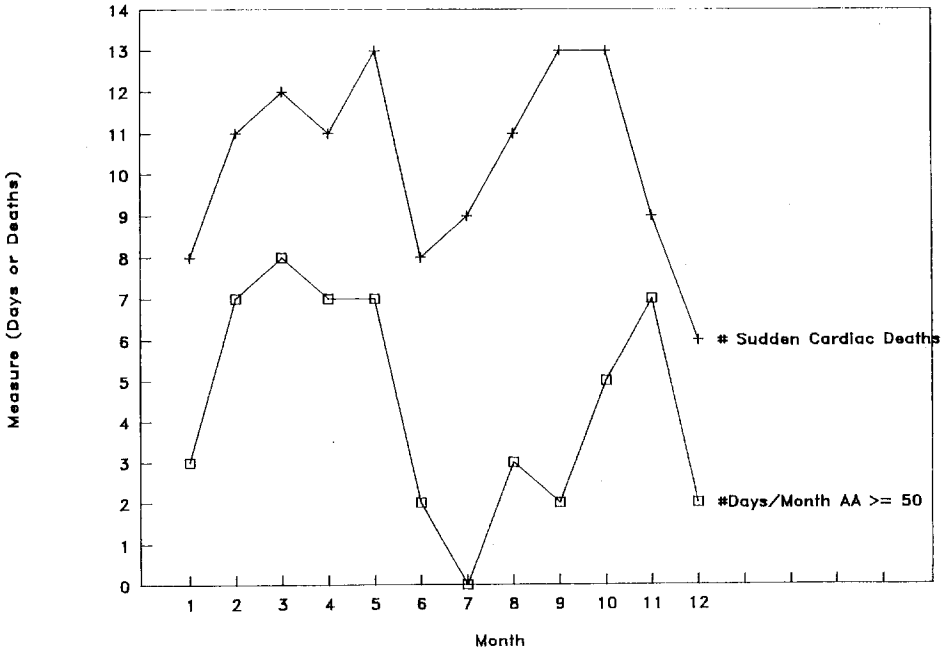

Fig. 3 Numbers of sudden cardiac deaths/month in epileptic patients (Leestma 1990) and the number of days in which average antipodal values >50 nT occurred per month for 1983

ues averaged 50 nT and when ssc began during the local night. Because the most violent magnetic storms frequently begin with an ssc (Mayaud 1973), the significant association between SUD and both the occurrence of an ssc and its onset during the beginning of local night, is expected. Even a crude analysis of Leestma's (1990) data indicated that the numbers of SUDEP increased during months that were associated with elevated geomagnetic activity. In fact the strongest and the only statistically significant correlation occurred between the number of SUDEP and the number of days per month in which the average aa value was equal to or greater than 50 nT.

The possibility that SUDs in epileptic organisms may be related to an increased risk of paroxysmal neuroelectrical activity in general during periods of enhanced geomagnetic activity was indicated by the two components of Experiment II. The incidence of nightly seizures for epileptic rats was positively correlated with the magnitude of aa values. Both forelimb clonus with secondary convulsions (as verified by videotape) and the incidence of thrashing and running seizures (as determined by vibration patterns) exhibited correlations of between +0.45 and +0.65 with the magnitude of the aa values of the same or previous day.

The relationship between the number of seizures and geomagnetic amplitude was not linear but exhibited a threshold of about 50 nT. The finding that none of the rats in the first two series (i.e., 8 rats) died suddenly is likely to be a proportional artifact since even in the major study the incidence of mortality during a 6 month period was about 1:50. In part 2 of Experiment II, which involved the daily assessment (29 days) of 45 healthy rats with a history of chronic seizures, only 1 rat died suddenly during the one and only night of a sudden, magnetic storm commencement.

The results of the present study are commensurate with our working hypothesis that cardiac arrhythmia, secondary to disruption between amygdaloid-paraventricular hypothalamic and insular pathways, is the catastrophic trigger to SUD. As has been emphasized by Leestma (1990) the absence of conspicuous anatomical explanations for SUDEPs suggests that death involves cardiovascular failure. Cardiac arrhythmias have been described of very common occurrence during seizures, especially those with tonic-clonic convulsions. The fact that arrhythmias (e.g., bradycardia) are associated with a seizure has been indicated by their presence only after the animal has been electrically kindled (Goodman et al. 1990).

During the first 24 h after the induction of seizures by lithium and pilocarpine, rats have frequently exhibited periods of arrhythmia that occasionally precede either strong bradycardia or sudden cessation and death (Harrigan et al. 1994). The effect is gradual, being markedly attenuated by acepromazine, and very similar to the results reported by Oppenheimer et al. (1991). It was found that continuous stimulation of a portion of the insula (Cechetto and Saper 1987), induced by direct electrical feedback from the QRS component of the electrocardiogram, also induced fatal cardiac arrhythmias. Our results have indicated that an electrical phase-shift ("uncoupling") between the normally coordinated basolateral amygdaloid-insular-central amygdaloid pathways to the paraventricular hypothalamus and solitary nucleus encourages arrhythmia. In view of the marked consistency in the spatial distribution of both the subtypes and magnitudes of different classes of receptors that have been found within the rat and human brain (Mendelsohn and Paxinos 1991), the probability of a species-specific artifact is quite small.

Currently, the most parsimonious mechanism by which sudden geomagnetic activity would encourage a fatal arrhythmia converges with and integrates contemporary knowledge. Melatonin is an endogenous anticonvulsant; central injections have been shown to evoke a rapid rise in inhibitory transmitters such as gamma-aminobutyric acid (GABA) within the hypothalamus (Rosenstein et al. 1989) while pinealectomy encourages epileptoid electrical discharges (Anton-Tay 1971). The initial stages of sudden suppression of melatonin by geomagnetic activity could decrease the threshold for paroxysmal discharges from the amygdaloid-hippocampal complex to the hypothalamus, which contains significant density of the melatonin receptor (Vanecek et al. 1987). Recent research has indicated that only 2 min of electrical stimulation of the multipotential paraventricular hypothalamus, which strongly influences descending sympathetic and parasympathetic fibers, also inhibits pineal melatonin synthesis (Olcese et al. 1987). The suppression would generate even greater limbic lability. Compromise of the cerebral cortices (particularly the temporal and frontal regions) because of acquired brain injury, would encourage the generalization of these discharges.

The relative effect of the sudden suppression of melatonin would be greater during the later portions of the night (midnight to 0600 hours) when REM periods predominate. They have been associated with small cyclic decreases in melatonin levels and with cardiac arrhythmias in heart patients (Rosenblatt et al. 1973). The rebound of melatonin suppression is less likely during the later hours of the local night because the noradrenalin fibers that stimulate the synthesis of this indoleamine decrease their activity. This time-dependence has been employed to explain why experimental and natural magnetic fields are primarily effective during the mid to later portions of the nocturnal phase (Yaga et al. 1993).

Epileptic rats that have received the same treatment as those reported in this study have exhibited substantial damage within the reticulata of the substantia nigra (Persinger et al. 1993). Those with the greatest damage are also most prone to spontaneous motor convulsions that are identical to those evoked by picrotoxin. Within the substantia nigra, gliosis and neuronal drop out increases with the duration of epilepsy (and does not occur in rats that have received lithium/pilocarpine but did not exhibit overt motor stereotypy) and is primarily concentrated in the region that receives thalamic input. This portion of the thalamus has also been shown to be vulnerable to

transneuronal degeneration subsequent to traumatic injury, particularly to the frontal and anterior temporal cortices (Povlishock and Coburn 1990). Because this portion of the substantia nigra is considered a final impedance to the uncontrolled propagation of electrical discharges to different (and usually compartmentalized) efferent centers (Gale 1988), the loss of inhibitory neurons would be metaphorically analogous to vascular anastomosis.

Excitotoxic damage to these thalamic regions has been reported to affect cardiac conditioning (Buchanan and Thompson 1989) and has been shown directly to produce pathological changes within cardiac tissue (Rockhold et al. 1990). If such pathology shares an etiology similar to that producing the cardiomegaly within SUDEP (Leestma 1990), then there may be a specific combination of conditions that open the pathways to a fatal cardiac arrhythmia precipitated by a geomagnetically mediated, sudden decrease in nocturnal melatonin levels during dream sleep in human beings: (1) thalamic damage-evoked cardiovascular changes; (2) compromised reticulata of the substantia nigra (McNamara 1987); and (3) limbic electrical foci and corpus striatal lability secondary to generalized frontal/temporal cortical injury.

The most compelling explanation for the present observations is that elevated geomagnetic activity had induced suppression of circulating melatonin concentrations by inhibiting pineal melatonin synthesis (Wilson et al. 1989, 1990); the effect may be more pronounced in individuals who have abnormal elevations of nocturnal melatonin, such as women with functional amenorrhoea (Berga et al. 1988), or who are psychologically depressed. Exposure to experimental magnetic fields within the microTesla range for only 30 min has been sufficient to reduce nocturnal pineal melatonin concentrations by more than 50% in vivo (Olcese and Reuss 1986) and in vitro (Welker et al. 1983). One possible physical mechanism may involve a Ca^{++} cyclotron resonance effect upon the synthesizing enzyme (Lerchl et al. 1991b). Clearly, as recently shown by Yaga et al. (1993), melatonin depletion by exposure to a magnetic field (serial 1 min activation and 1 min deactivation of the coil for only 45 min) is maximum only during the peak of the nocturnal melatonin cycle occurring after midnight.

Despite the consistent assocation between SUD and enhanced geomagnetic activity in samples of both rat and human epileptics, the specific physical stimulus that initiates the hypothesized melatonin-suppression and subsequent fatal cardiac arrhythmia remains to be determined. Although the magnitude of the experimental magnetic fields that have been demonstrated to suppress nocturnal melatonin concentrations are more than 100 times that of natural geomagnetic variations with which SUD has been associated, the key (effective) parameters of the stimulus structure have not been isolated. The aa values are scalar quantities that reflect the amplitude of the disruption in the geomagnetic field. The results of this study strongly suggest that there is some specific magnetic field structure: perhaps a secondary "ripple", which like the modal electroencephalographic frequency, is crudely associated with the shift in cerebral steady state (d.c.) potentials or a concomitant physical stimulus that is more probable during periods when aa values exceed 50 nT or when sscs occur.

Whether this stimulus is simply a more effective disrupter of nocturnal melatonin or if any stimulus that disrupts this circadian pattern (e.g., brief exposure to artificial white light during the night cycle) can evoke arrhythmias must also be examined. If, as has been shown by Yaga et al. (1993), red light during the nocturnal phase is essential for the interaction between ambient magnetic fields and melatonin suppression, then a significant proportion of SUDs in the human population may be encouraged by this surprisingly common increment of the light spectra during nocturnal periods. Habituation to geomagnetic perturbations that exceed 40 to 50 nT during consecutive days would be expected because of the adjustment of neuroelectrical thresholds to the protracted suppression of melatonin. In the present study, epileptic rats responded maximally during the first 48 h after sudden increase in geomagnetic activity. This feature should be considered in future retrospective analyses of SUDEP.

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